UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/651,876 | 08/29/2003 | Kenneth F. Bastow | 5470.395 | 9346 |

20792 7590 11/09/2006

MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

| EXAMINER | |
|---|---|
| STITZEL, DAVID PAUL | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1616 | |

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/651,876 | BASTOW ET AL. | |
| | Examiner | Art Unit | |
| | David P. Stitzel, Esq. | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9 and 21* is/are pending in the application.

4a) Of the above claim(s) *3 and 6-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/03; 7/1/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## OFFICIAL ACTION

### *Acknowledgment of Receipt*

Receipt of the Applicants' Election, without traverse, of: Invention I, encompassing claims 1-9; human cytomegalovirus as the patentably distinct species of herpesvirus of the Family Herpesviridae; and 1-hydroxy-3-isopropoxy-7-methoxyacridone (a.k.a., 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one) as the patentably distinct species of a compound of formula I; which was filed on September 29, 2006, in response to the Official Action dated September 1, 2006, is acknowledged.

### *Status of Claims*

Claims 10-20 were canceled, and claim 21 was added, by an amendment that accompanied the aforementioned Election. In addition, claims 3 and 6-9 are withdrawn from further consideration as being directed to a non-elected invention. As a result, claims 1, 2, 4, 5 and 21 are therefore examined herein on the merits for patentability.

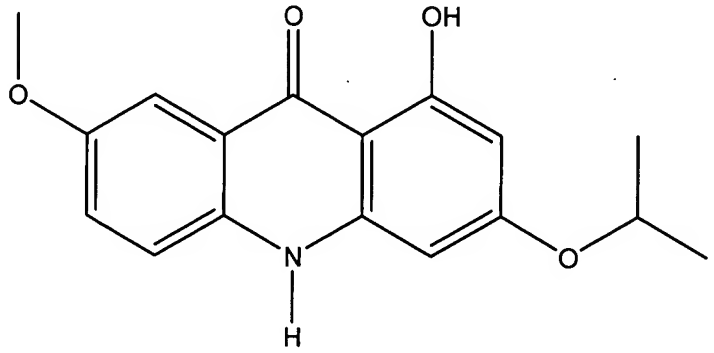
### *Claim Rejections - 35 U.S.C. § 102*

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102, which forms the basis of the anticipation rejections as set forth under this particular section of the Official Action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 2, 4, 5 and 21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lowden CT, "Antiviral Acridones," Dissertation Abstracts International, Vol. 62, No. 3B, p. 1398 (Order No. AAI3007835, pp. 1-147) (2001) (hereinafter the Lowden dissertation publication).

With respect to claims 1, 2, 4, 5 and 21 of the instant application, the Lowden dissertation publication teaches a method of treating human cytomegalovirus (HCMV) infection, wherein said method comprises administering 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one (a.k.a., 1-hydroxy-3-isopropoxy-7-methoxyacridone), the structure of which is illustrated in greater detail hereinbelow:




1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one
(a.k.a., 1-hydroxy-3-isopropoxy-7-methoxyacridone)

(abstract; page 1, lines 10-23; page 2, lines 1-3; page 4, Figure 1 and lines 1-3 and 8-10; page 5, lines 2 and 3; page 26, Figure 8, compound 4; page 37, lines 1, 5-7 and 9; page 38, Table 4, compound 4; page 40, Figure 10, compound 4; page 77, Table 8, compound 4; page 81, Table 9, ***compound 38***; page 83, last paragraph, lines 1-4; page 84, lines 1-11 and Table 10, ***active compound 38***; page 117, last paragraph, lines 1 and 2; page 118, lines 1-21; page 131, lines 14-16, 22 and 23; page 132, lines 1 and 2; page 133, last paragraph; page 135, last paragraph).

One of ordinary skill in the art at the time the instant application was filed would have reasonably anticipated that said 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one active acridone derivative would be effective in treating subjects (e.g., mammalian) infected with HCMV, especially in light of the teachings of the Lowden dissertation publication, which states in relevant part that the aforementioned *in vitro* "plaque assay is the accepted standard approach for measuring anti-

HCMV activity," and that a number of said acridone derivatives exhibit *in vitro* activity profiles that rival HCMV drugs currently on the market (page 2, lines 1-3; page 81, Table 9, ***compound 38***; page 84, Table 10, ***active compound 38***; page 131, lines 15 and 16; page 133, last paragraph; page 135, last paragraph).

***Claim Rejections - 35 U.S.C. § 103***

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

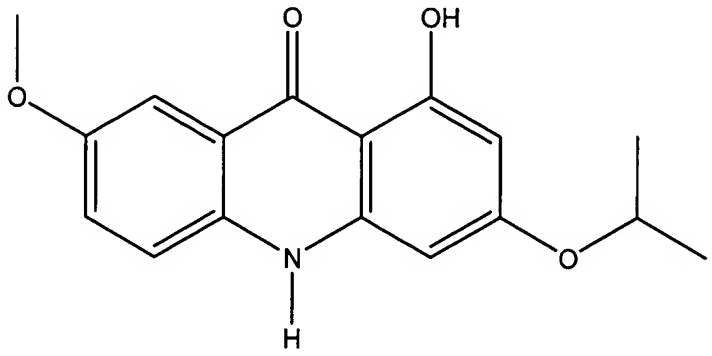
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1, 2, 4, 5 and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lowden CT, "Antiviral Acridones," Dissertation Abstracts International, Vol. 62, No. 3B, p. 1398 (Order No. AAI3007835, pp. 1-147) (2001) (hereinafter the Lowden dissertation publication).

With respect to claims 1, 2, 4, 5 and 21 of the instant application, the Lowden dissertation publication teaches an *in vitro* method of inhibiting human cytomegalovirus (HCMV) replication by

reducing HCMV plaque formation in human embryonic lung (HEL) cells infected with HCMV, wherein said method comprises administering to said HCMV infected HEL cells 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one (a.k.a., 1-hydroxy-3-isopropoxy-7-methoxyacridone), the structure of which is illustrated in greater detail hereinbelow:




1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one
(a.k.a., 1-hydroxy-3-isopropoxy-7-methoxyacridone)

(abstract; page 1, lines 10-23; page 2, lines 1-3; page 4, Figure 1 and lines 1-3 and 8-10; page 5, lines 2 and 3; page 26, Figure 8, compound 4; page 37, lines 1, 5-7 and 9; page 38, Table 4, compound 4; page 40, Figure 10, compound 4; page 77, Table 8, compound 4; page 81, Table 9, ***compound 38***; page 83, last paragraph, lines 1-4; page 84, lines 1-11 and Table 10, ***active compound 38***; page 117, last paragraph, lines 1 and 2; page 118, lines 1-21; page 131, lines 14-16, 22 and 23; page 132, lines 1 and 2; page 133, last paragraph; page 135, last paragraph).

The Lowden dissertation publication does not explicitly teach an *in vivo* method of treating an HCMV infected subject (e.g., mammalian) by inhibiting HCMV replication therein comprising administering 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one to said HCMV infected subject in need thereof, as instantly claimed in claim 1.

However, the Lowden dissertation publication teaches an *in vitro* method of inhibiting HCMV replication by reducing HCMV plaque formation in HEL cells infected with HCMV, wherein said

method comprises administering to said HCMV infected HEL cells 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one (a.k.a., 1-hydroxy-3-isopropoxy-7-methoxyacridone). In addition, the Lowden dissertation publication teaches that the aforementioned *in vitro* "plaque assay is the accepted standard approach for measuring anti-HCMV activity" (page 131, lines 15 and 16).

Moreover, the instant application likewise does not appear to provide even a scintilla of *in vivo* scientific experimental data with respect to an *in vivo* method of treating an HCMV infected subject (e.g., mammalian) by inhibiting HCMV replication therein comprising administering 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one to said HCMV infected subject in need thereof. In fact, the only scientific experimental data provided within the instant specification appears to be based on the same *in vitro* plaque assay taught in the Applicant's dissertation, namely the Lowden dissertation publication. See U.S. Pre-Grant Patent Application Publication 2005/0049273, which is the published version of the instant specification (hereinafter the Bastow '273 publication) (paragraphs [0023]-[0027], [0106]-[0108], [0113] and [0114]); and the Lowden dissertation publication (page 2, lines 1-3; page 81, Table 9, ***compound 38***; page 83, last paragraph, lines 1-4; page 84, lines 1-11 and Table 10, ***active compound 38***; page 117, last paragraph, lines 1 and 2; page 118, lines 1-21; page 131, lines 14-16, 22 and 23; page 132, lines 1 and 2; page 133, last paragraph; page 135, last paragraph).

The Lowden dissertation publication teaches not only that the aforementioned *in vitro* "plaque assay is the accepted standard approach for measuring anti-HCMV activity," but also that a number of said acridone derivatives exhibit *in vitro* activity profiles that rival HCMV drugs currently on the market and explicitly suggests that *in vivo* models should be conducted in the future with respect to activity, toxicity and routes of administration of said active acridone derivatives (page 2, lines 1-3; page 81, Table 9, ***compound 38***; page 84, Table 10, ***active compound 38***; page 131, lines 15 and 16; page 133, last paragraph; page 135, last paragraph). Therefore, it would have been prima facie obvious

to one of ordinary skill in the art at the time the instant application was filed to conduct *in vivo* scientific experiments comprising administering 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one, which is an active acridone derivative, to HCMV infected subjects (e.g., HCMV infected mammals including, mice, rats and eventually humans). One of ordinary skill in the art would have been motivated to conduct *in vivo* scientific experiments comprising administering 1-hydroxy-3-isopropoxy-7-methoxyacridin-9(10*H*)-one, which is an active acridone derivative, to HCMV infected subjects (e.g., HCMV infected mammals including, mice, rats and eventually humans) in need thereof, so as to determine the therapeutic efficacy of anti-HCMV activity within said HCMV infected subjects.

***Comment Regarding 35 U.S.C. § 112, First Paragraph***

It should be mentioned that compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is in fact disclosed, but rather, whether the invention is otherwise disclosed in such manner that one of ordinary skill in the art would be able to practice the invention without an undue amount of experimentation. See MPEP §2164.02. An example may be "working" or "prophetic" in nature. *Id.* A working example is based on work actually performed, whereas a prophetic example describes an embodiment of the invention based on predicted results as opposed to work actually conducted or results actually achieved. *Id.* The issue of "correlation," which refers to the relationship between *in vitro* or *in vivo* animal model assays and a disclosed or claimed method of use, is related to the issue of the presence or absence of working examples. *Id.* An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention. *Id.* In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the Examiner has evidence to the contrary. *Id.* Even with such evidence

in hand, the Examiner must weigh the evidence for and against correlation and decide whether one of ordinary skill in the art would accept the model as reasonably correlating to the condition. *Id.* A rigorous or an invariable exact correlation is not required when based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and the disclosure of pharmacological activity is reasonable based upon the probative evidence. *Id.* In the instant case, the Lowden dissertation publication teaches that the aforementioned *in vitro* "plaque assay is the accepted standard approach for measuring anti-HCMV activity," and that a number of said acridone derivatives exhibit *in vitro* activity profiles that rival HCMV drugs currently on the market (page 2, lines 1-3; page 81, Table 9, compound 38; page 84, Table 10, active compound 38; page 131, lines 15 and 16; page 133, last paragraph; page 135, last paragraph).

***Conclusion***

Claims 1, 2, 4, 5 and 21 are rejected because the claimed invention would have been anticipated and/or prima facie obvious to one of ordinary skill in the art at the time the invention was made since each and every element of the claimed invention, as a whole, is disclosed in and/or would have been reasonably suggested by the teachings of the cited prior art references.

***Contact Information***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to David P. Stitzel, M.S., Esq., whose telephone number is 571-272-8508. The Examiner can normally be reached on Monday-Friday, from 7:30AM-6:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Johann Richter, Ph.D., Esq., can be reached at 571-272-0646. The central fax number for the USPTO is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published patent applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished patent applications is only available through Private PAIR. For more information about the PAIR system, please see http://pair-direct.uspto.gov. Should you have questions about acquiring access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*David P. Stitzel, M.S., Esq.*
*Patent Examiner*
*Technology Center 1600*
*Group Art Unit 1616*

*Johann Richter, Ph.D., Esq.*
*Supervisory Patent Examiner*
*Technology Center 1600*
*Group Art Unit 1616*